DETAILED ACTION

1. Amendment and response filed by applicants dated Dec. 20, 2007 have been entered and considered carefully.

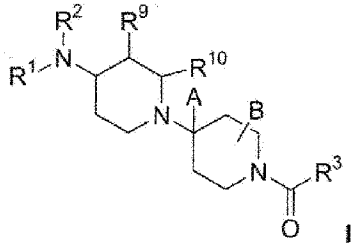
Claims 1-20, 31-40 have been canceled. Claims 21-30 are pending.

2. ***Examiner's Amendment***

Authorization for this examiner's amendment was given in a telephone interview with Dr. Krishna G. Banetjee on Mar. 18, 2008.

In claim 21, the scope of R2 is limited to those of example 2, p.50-63.

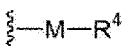
21. (Currently amended) A compound represented by the structural formula I



I

or a pharmaceutically acceptable salt ~~or, solvate~~ thereof; wherein:

$\mathbf{R^1}$ is



:

R^2 is [arylalkyl] **benzyl or 4-fluorobenzyl**;

R^3 is selected from the group consisting of 6-membered heteroaryl, and 6-membered heteroaryl-N-oxide, wherein said. 6-membered heteroaryl or heteroaryI-N-oxide is pyrimidine or pyrimidine-N-oxide respectively, each of which is optionally substituted with 1-4 substituents which can be the same or different and. are independently selected from the group consisting of R^{11}, R^{12}, R^{13}, R^{14} and R^{15};

R^4 is 1-3 substituents selected from the group consisting of H, halo, alkyl, haloalkyt, alkoxy, cycloalkyl, amide, CF_3, OCF_3, aryl, heteroaryl, $-XR^7$, -CN, $-CO_2H$, $-CO_2R^{22}$, R^8-aryl(C_1-C_6)alky-, R^8-heteroaryl(C_1-C_6)alkyl-, $-C(O)NR^{21}R^{22}$,$-C(O)NH_2$, wherein R^4 can be the same or different and is independently selected when there is more than one R^4 present;

R^7 is selected from the group consisting of aryl substituted aryl, heteroaryl, alkyl, haloalkyl and cycloalky!;

R^8 is 1, 2 or 3 substituents selected from the group consisting of H, halo, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy,-CF_3,-OCF_3, $CH_3C(O)$-, -CN., CH_3SO_2-, CF_3SO_2- and -NH_2, wherein R^8 can be the same or different and is independently selected when there are more than one R^8 present;

R^9, R^{10} and B can be the same or different and are each independently selected from the group consisting of hydrogen, $(C_1$-$C_6)$alkyl, and -$(C_1$-$C_6)$heteroalkyl;

R^{11} and R^{12} can be the same or different and are each independently selected from the group consisting of -$(C_1$-$C_6)$alkyl, -$(C_1$-$C_6)$haloalkyl, halogen, -$NR^{19}R^{26,}$ -OH, CF_3,-OCH_3,-O-acyl, and-OCF_3;

R^{13} is selected from the group consisting of hydrogen, $R^{11,}$ H, phenyl, NO_2, -CN,-CH_2F, -CHF_2, -CHO, -CH=NOR^{19}, pyridyl-N-oxide, pyrimidinyl, pyrazinyl, N(R^{20})CO N $R^{20}R^{21}$, -NHCONH (chloro-$(C_1$-$C_6)$alkyl), -NHCONH ($(C_3$-$C_{10})$-cycloalkyl$(C_1$-$C_6)$alkyl), -NHCO$(C_1$-$C_6)$alkyl, -NHCOCF_3, -NHCOCF_3, -NHSO_2N($(C_1$-$C_6)$alkyl, -N$HSO_2(C_1$-$C_6)$alkyl,-N(SO_2CF_3)2,-N$HCO_2(C_1$-$C_6)$alkyl, $(C_3$-$C_{10})$cycloalkyl,-SR^{22}, $SOR^{22,}$-SO_2R^{22}, -SO_2N H$(C_1$-$C_6)$alkyl, -$OSO_2(C_1$-$C_6)$alkyl, -OSO_2CF_3, hydroxy$(C_1$-$C_6)$alkyl, -$CONR^{19}R^{20,}$-CON $(CH_2CH_2$-O –$CH_3)_2$, -OCONH$(C_1$-$C_6)$alkyl, -CO_2R^{19}, $Si(CH_3)_3$ and -$B(OC(CH_3)_2)_2$;

R^{14} is selected from the group consisting of $(C_1$-$C_6)$alkyl, -$(C_1$-$C_6)$haloalkyl -NH_2 and R^{15}-phenyl;

R^{15} is 1-3 substituents selected from the group consisting of hydrogen, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, -CF_3, -$CO_2R^{20,}$-CN, $(C_1$-$C_6)$alkoxy and halogen; wherein R^{15} can be the same or different and is independently selected when there are more than one R^{15} present;

$R^{19,}$ R^{20} and R^{21} can each be the same or different and are each independently selected from the group consisting of H, $(C_1$-$C_6)$alkyl and $(C_3$-$C_6)$cycloalkyl;

R^{22} is selected from the group consisting of -$(C_1$-$C_6)$alkyl, -$(C_1$-$C_6)$haloalkyl, -$(C_2$-$C_6)$hydroxyalkyl, $(C_2$-$C_6)$alkylene, $(C_3$-$C_6)$cycloalkyl, aryl and aryl$(C_1$-$C_6)$alkyl-;

A is selected from the group consisting of H, $(C_1$-$C_6)$alkyl, and $(C_2$-$C_6)$alkenyl,

M is aryl optionally substituted with R^4; and

X is selected from the group consisting of CH_2, SO_2, SO, S, and O, with the following proviso: when R^1 is phenyl., or naphthyl, R^2 cannot be H, $(C_1$-$C_6)$alkyf or -C(O)- $(C_1$-$C_6)$alky.

There are duplicate claims 28-29. The **first set** claims 28-29 are canceled.

3. ***Reason for Allowance***

The following is an examiner's statement of reasons for allowance:

Applicants have provided evidence that in Table 2 of the Declaration filed on Mar. 8, 2007, the comparison between example 72 and the reference compound of the prior art showed that the dimethylpyrimidyl compounds and dimethylphenyl compounds of the prior art do have similar activity for which an prima facie obviousness was established in the office action. However, example 9, which showed that when R^2 is benzyl such compounds have unexpected property in that it has reduced plasma protein binding thus higher efficiency in vivo (see p.4-5 declaration). Applicants have also limited the claims to the compounds commensurate to this unexpected result that is R^2 being benzyl or fluorobenzyl as disclosed in example 2 (p.50-63). Claims 21-30 as currently amended are allowed.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang, Ph. D. whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Mar. 24, 2008

/Celia Chang/
Primary Examiner
Art Unit 1625